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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Glauco P. Tocchini-Valentini

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QUARLES & BRADY LLP
411 E. WISCONSIN AVENUE
SUITE 2040
MILWAUKEE, WI 53202-4497

EXAMINER

SHIN, DANA H

ART UNIT

PAPER NUMBER

1635

MAIL DATE

DELIVERY MODE

11/17/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/821,777	TOCCHINI-VALENTINI ET AL.	
	Examiner	Art Unit	
	DANA SHIN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 August 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 4-23 is/are pending in the application.
- 4a) Of the above claim(s) 18-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 4-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>8-19-2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 19, 2008 has been entered.

Status of Claims

Currently, claims 1 and 4-23 are pending in the instant application. Claims 18-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. See applicant's election filed on March 8, 2007. Accordingly, claims 1 and 4-17 are currently under examination on the merits.

Response to Arguments

Applicant's arguments and the declaration under 37 C.F.R. §1.132 filed with the RCE on August 19, 2008 with respect to claims 1 and 4-17 have been considered but are moot in view of the new ground(s) of rejection. See below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 4-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abelson et al. (*The Journal of Biological Chemistry*, 1998, 273:12685-12688) in view of Diener et al. (*Molecular Cell*, 1998, 1:883-894, applicant's citation) and Reyes et al. (*Analytical Chemistry*, 1987, 166:90-106).

The claims are drawn to a method of cleaving a target RNA molecule comprising exposing the target molecule to an eukaryotic tRNA splicing endonuclease or a heterologous archaeal tRNA splicing endonuclease, wherein the target molecule is in the BHB conformation, wherein the cleavage occurs within the BHB having a G/A dinucleotide and a U/A dinucleotide, and the target molecule does not comprise a tRNA structure, wherein BHB conformation is obtained by hybridizing the target molecule with an oligonucleotide designed to form a BHB

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conformation, wherein the target molecule is an mRNA, the cleavage occurs within a cell *in vitro* and *in vivo*, wherein the cell is a mammalian cell.

Abelson et al. teach that tRNA endonuclease-mediated target tRNA splicing occurs in the splice sites found in an “absolutely conserved structural motif consisting of two loops of three bases separated by a four-base pair helix, the bulge-helix-bulge (BHB) motif” (see page 12685), which are conserved in both the Eukarya and the Archaea: “both the eukaryal and archaeal endonucleases can accurately cleave a universal substrate containing the BHB motif” (emphasis added). See page 12688. Abelson et al. do not teach a method of tRNA endonuclease-mediated cleavage of a non-tRNA substrate, which is artificially induced to form the “absolutely conserved” BHB motif at the U/A and G/A dinucleotides.

Diener et al. teach that the 3' cleavage site of the BHB motif in pre-tRNA contains U/A dinucleotide, wherein the cleavage occurs between the U and A and the 5' cleavage site of the BHB motif in the pre-tRNA contains G/A dinucleotide, wherein the cleavage occurs between the G and A. See the entire reference including Figure 1.

Reyes et al. teach a method of synthesizing an artificial RNA oligonucleotide substrate for *in vitro* splicing by a tRNA splicing endonuclease. They teach that the synthesized RNA oligonucleotide substrate contains the 5' splice cleavage site containing the G/A dinucleotide and the 3' splice cleavage site containing the U/A dinucleotide and that the synthetic RNA is accurately cleaved at the G/A 5' splice site and at the U/A 3' splice site. Hence, Reyes et al. demonstrate structure-based (G/A and U/A containing cloverleaf structures) substrate recognition and subsequent splicing by a tRNA splicing endonuclease. See the entire reference including Figure 2 and Table 2.

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It would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the inherent biological property of tRNA splicing endonuclease (the BHB motif structure-based splicing or cleavage of a target RNA oligonucleotide substrate as taught by Abelson et al. and Diener et al.) to cleave or splice an artificially synthesized, non-tRNA oligonucleotide substrate that contains the BHB motif, each containing the G/A and U/A dinucleotide in light of the teachings of Reyes et al.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success, because Abelson et al. taught that the BHB motif structure-based splicing or cleavage of a target RNA oligonucleotide substrate is a conserved, absolute biological mechanism of a tRNA splicing endonuclease and therefore suggested that the tRNA splicing endonuclease can cleave any substrate ("universal substrate") containing the BHB motif, and particularly because Reyes et al. demonstrated that one can synthesize a tRNA splicing endonuclease substrate by synthesizing an oligonucleotide to form a cloverleaf motif containing the required G/A and U/A splice dinucleotide sequences, which are the very 5' and 3' splice sites in the BHB motif cleaved by a eukaryotic or archael tRNA splicing endonuclease, as taught by Diener et al. Since tRNA splicing endonuclease-mediated target RNA cleavage was not only suggested but also demonstrated to occur in any synthetic oligonucleotide substrate having proper structures that can be recognized by the tRNA splicing endonuclease (i.e., BHB or cloverleaf motif containing a G/A 5' splice site and a U/A 3' splice site) as evidenced by the teachings of Abelson et al. and Reyes et al., it would have been obvious to one of ordinary skill in the art that the tRNA splicing endonuclease-mediated target cleavage is not restricted to tRNA substrates, but is applicable to non-tRNA substrates as long as the non-tRNA synthetic substrates contain the BHB motif with proper splice recognition sites. Since the knowledge and skills

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required to arrive at the claimed invention were within the technical grasp of one of ordinary skill in the art at the time of the invention, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, from 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

/J. E. Angell/
Primary Examiner, Art Unit 1635